



Are gastrointestinal problems, nutritional care, and nutritional care needs associated with quality of life in patients with advanced cancer? Results of the observational eQuiPe study

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Abstract

Purpose To assess the association of gastrointestinal problems, received nutritional care, and nutritional care needs with quality of life (QoL) in patients with advanced cancer.

Methods A cross-sectional analysis within the observational prospective eQuiPe cohort study on experienced quality of care and QoL in patients with advanced cancer was performed. QoL and gastrointestinal problems were measured using the European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire (EORTC QLQ)-C30. Received nutritional care (yes/no) and nutritional care needs (yes/a little bit/no) were measured by two questions. Gastrointestinal problems were categorized as clinically important based on the Giesinger thresholds. Univariable and multivariable linear regression analyses adjusted for age, gender, and treatment were used to analyze the association of gastrointestinal problems, received nutritional care, and nutritional care needs with QoL.

Results Half of the 1080 patients with advanced cancer had clinically important gastrointestinal problems, 17% experienced nutritional care needs, and 14% received nutritional care. Multivariable analyses revealed that the presence of clinically important gastrointestinal problems (β (95% CI): -13.0 (-15.6 ; -10.4)), received nutritional care (β (95% CI): -5.1 (-8.5 ; -1.7)), and nutritional care needs (β (95% CI): -8.7 (-11.9 ; -5.5)) were associated with a low QoL.

Conclusion Many patients with advanced cancer experience gastrointestinal problems, while only few patients receive nutritional care. These gastrointestinal problems, nutritional care needs, and nutritional care are associated with lower QoL, probably due to reversed causality or the irreversible nature of these problems in the palliative phase. More research on the relation of nutritional care, gastrointestinal problems, and QoL is needed to optimize nutritional support in end-of-life care.

Keywords Advanced cancer · Gastrointestinal problems · Nutritional care needs · Nutritional care · Quality of life · Palliative care

Introduction

In 2020, over 19 million new cases of cancer were diagnosed worldwide [1]. Cancer is still a leading cause of death, accounting for approximately 10 million deaths per year [1]. In the Netherlands, the estimated number of new cancer diagnoses is 115,000 per year [2] and 21,000 persons

with a solid cancer diagnosis already have distant metastases at diagnosis. In addition, there are over 38,000 patients annually who develop distant metastases and require palliative care [3]. Studies have shown that early palliative care improves quality of life (QoL) in patients with advanced cancer [4]. In the course of progression of disease, this care gradually moves from a disease-oriented perspective to a more symptom-oriented treatment only [5].

Patients with advanced cancer often suffer from disease- and treatment-related gastrointestinal problems. The most common gastrointestinal symptoms are appetite loss (53%), dry mouth (40%), constipation (34%), and nausea (31%) [6].

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Literature shows that these gastrointestinal problems are all associated with lower QoL [7, 8]. From the gastrointestinal problems, appetite loss was most predictive of overall QoL [7].

Due to the high prevalence of gastrointestinal symptoms and weight loss in patients with advanced cancer, nutritional care needs might be high. In line with this, Amano et al. showed that 76% of terminally ill patients had general unmet needs for nutrition therapy for cancer cachexia, and 61% indicated that they needed specific support by health care professionals such as attention and explanation concerning their distress about eating [9].

The role of dieticians in palliative oncology care is important. Dieticians can have a positive impact through nutritional evaluation, counseling, psychosocial support, follow-up, and nutritional interventions [10]. When the focus of palliative care is still on disease-modifying treatment, dieticians contribute to the identification of malnutrition, the treatment of weight loss, and diminishing gastrointestinal problems, which may improve QoL [11]. However, when palliative care shifts from disease-modifying treatment towards the alleviation of symptom burden only, also the role of nutritional care will change in enhancing patient comfort and quality of life.

Few studies have investigated the association between nutritional care needs and nutritional care with QoL in patients with advanced cancer. However, a narrative review described that nutritional care should be integrated into the care for patients with advanced cancer because limited access to nutritional care is a major source of distress for patients and family members [11]. Moreover, some studies have shown the potential benefits of nutritional care, including preventing bedsores, improving performance status in advanced cancer patients [12, 13], but no study has specifically looked at its relation with QoL. Therefore, the aim of this study was to investigate the association of gastrointestinal problems, received nutritional care, and nutritional care needs with QoL in patients with advanced cancer.

Methods

Study design

A secondary analysis was conducted, using the baseline data of the observational prospective eQuiPe cohort study on the experienced quality of care and QoL in patients with advanced cancer and their relatives [14]. Patients were identified and recruited in the departments of medical oncology, pulmonology, or urology of more than 40 hospitals in the Netherlands. Participants in this analysis were recruited between November 2017 and January 2020, and completed questionnaires using the system of the Patient Reported

Outcomes Following Initial treatment and Long-term Evaluation of Survivorship (PROFILES) registry. PROFILES is a registry, linked to the Netherlands Cancer Registry (NCR), to collect data of cancer patients and noncancer controls to estimate the impact of cancer, beyond normal aging and the presence of comorbidities. PROFILES enables the investigation of the physical and psychosocial impact of cancer and its treatment in large groups of patients with cancer and is acknowledged as a unique infrastructure for survivorship research [15]. The eQuiPe study was exempted from full medical ethical review according to the Dutch Medical Research Involving Human Subjects Act (WMO), declared by the Medical Research Ethics Committee of the Antoni van Leeuwenhoek hospital (METC17.1491). Informed consent was obtained from all participants.

Participants

All adult patients with advanced cancer were eligible. Advanced cancer was defined as the presence of a solid metastasized tumor, including both synchronous (at diagnose) and metachronous distant metastases without possibilities for cure [14]. Additional criteria for patients with breast cancer were the presence of metastases in multiple organ systems. For patients with metastasized prostate cancer, the tumor had to be castrate-resistant. Patients also had to be able to complete Dutch questionnaires.

Measures

Quality of life

Quality of life (QoL) was assessed using the validated European Organization for the Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 items (EORTC-QLQ-C30) questionnaire [16]. The subscale global QoL was used, consisting of the two following items: “How would you rate your overall health during the past week?” and “How would you rate your overall quality of life during the past week?” with answer options ranging from 1 (very poor) to 7 (excellent). The presence of gastrointestinal problems was derived from the following items and scales of the EORTC-QLQ-C30: appetite loss, constipation, diarrhea, and nausea/vomiting. The mean scores of the subscales of nausea and vomiting and global QoL and the item scores were linearly transformed to a 0–100 scale, with a higher score implying a higher level of symptoms or a higher global quality of life, respectively.

Based on the thresholds for clinical importance of Giesinger et al. [17] for each symptom (score above 8 for nausea/vomiting, above 17 for diarrhea, and above 50 for appetite loss and constipation), patients were categorized into three categories: “No gastrointestinal problems

present” (all scores were 0), “Non-clinically important gastrointestinal problems present” (no score higher than the thresholds, but at least one symptom was present), and “Clinically important gastrointestinal problems present” (at least one score higher than the thresholds).

Nutritional care and care needs

Nutritional care by a dietician was assessed with the question “Have you consulted a dietician in the last month?” and the answer options were yes or no. A single item on need for information regarding nutritional care was added to the validated Problems and Needs in Palliative Care short version questionnaire (PNPC-sv) [18]. Patients were asked whether this was a problem, using “yes,” “a little bit,” and “no.” The responses “yes” and “a little bit” were combined. This additional question was tested using the “think-aloud” method and yielded good results in terms of comprehensiveness and appropriateness [14].

Sociodemographic and clinical characteristics

Age, sex, relationship status (having a partner or not), and education were self-reported. Education was categorized into low (no education or primary school), intermediate (lower general secondary education, vocational training or equivalent), and high (pre-university education, high vocational training, university). Tumor type was extracted from the NCR. Moreover, patients were also asked to self-report whether they had received treatment in the last month. The response options included radiotherapy, chemotherapy, surgery, targeted therapy, immunotherapy, or a combination of these treatments.

Statistical methods

Descriptive statistics and univariable linear regression analyses were conducted with gastrointestinal problems, received nutritional care, and nutritional care needs as separate independent variables, and QoL as dependent variable. Dummy variables were used for the categorical variable regarding gastrointestinal problems with the category “No gastrointestinal problems” being the reference category. Next, a multivariable linear regression model was fitted combining the previously mentioned variables and adjusting for age, sex, and treatment, which were selected a priori as confounders. All statistical analyses were performed using STATA version 16 (StataCorp, College Station, TX 77845, USA). p values <0.05 were considered statistically significant.

Results

In total, 1695 eligible patients with advanced cancer were invited to participate by phone, 1440 (85%) were enrolled in the study, and 1103 (65%) patients completed the baseline questionnaire. Due to missing data on the global QoL scale, 23 patients had to be excluded, leaving 1080 patients for further analysis (Fig. 1). The mean age of participants was 65 years (SD 9.8), 51% was male, and 74% had received anti-tumor treatment during the past month (Table 1).

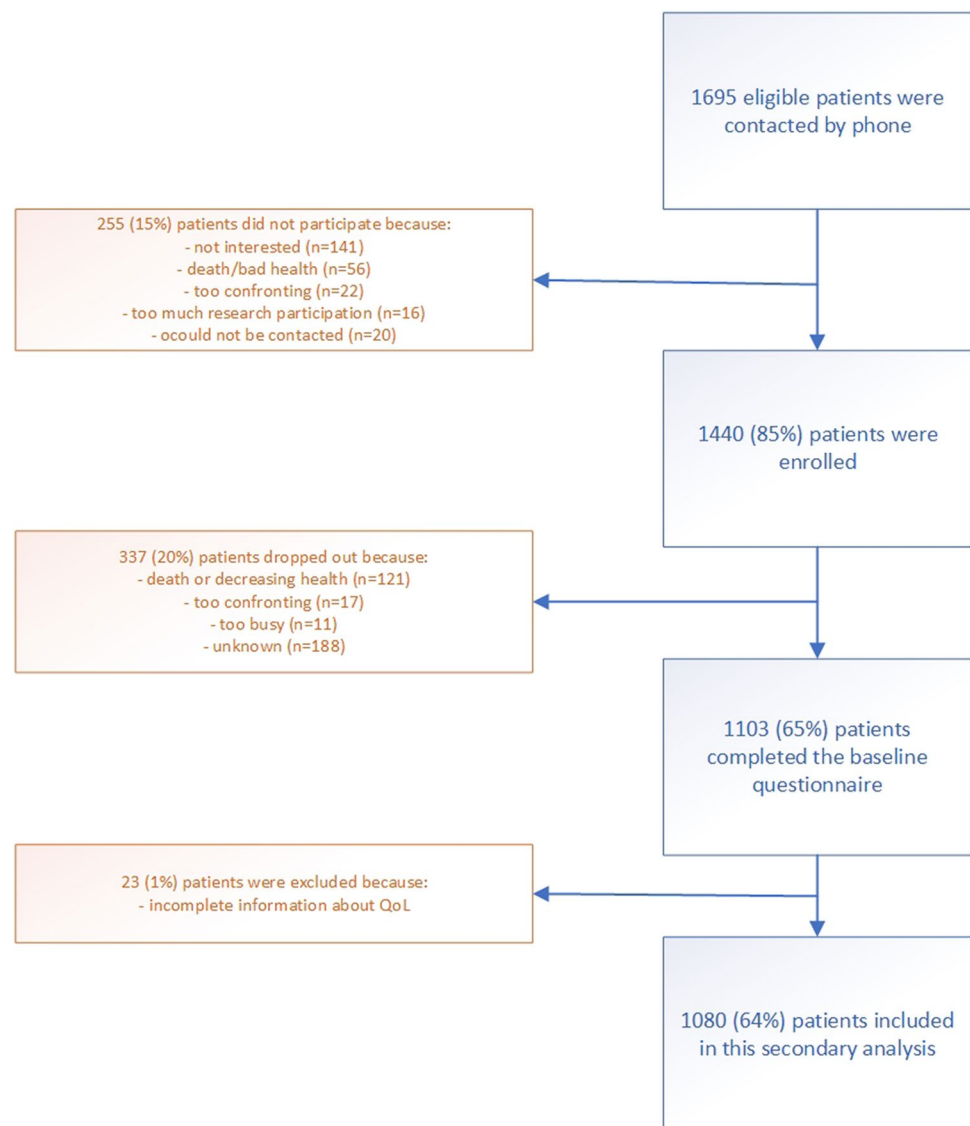
Gastrointestinal problems, nutritional care, and nutritional care needs

Half of all patients had at least one clinically important gastrointestinal problem (nausea/vomiting, loss of appetite, constipation, or diarrhea) whereas 16% reported ≥ 1 non-clinically important gastrointestinal problems, and 34% reported no gastrointestinal problems. The mean scores were 9.4 (SD 18) for nausea/vomiting, 19 (SD 27) for appetite loss, 13 (SD 23) for constipation, and 12 (SD 23) for diarrhea.

Fourteen percent of all patients had received nutritional care by a dietician during the past month. Patients with clinically important gastrointestinal problems more often received nutritional care compared to patients with no clinically important problems or with no gastrointestinal problems at all, respectively 19%, 14%, and 8% ($p < 0.05$) (Table 1). Of all patients, 176 patients (17%) had nutritional care needs. The nutritional care needs were similar in patients receiving nutritional care compared to patients receiving no nutritional care. Patients with clinically important gastrointestinal problems more often had (some) nutritional care needs compared to patients with no clinically important problems or with no gastrointestinal problems at all, respectively 21%, 16%, and 12% ($p < 0.05$) (Table 1).

Association between gastrointestinal problems, nutritional care, and nutritional care needs with QoL

Quality of life was lower in patients with clinically important gastrointestinal problems compared to non-clinically relevant or no gastrointestinal problems, respectively 61.9 (SD 20), 69.4 (SD 19.1), and 76 (SD 17.2). Of the four questions on gastrointestinal problems of the EORTC-QLQ-C30, appetite loss had the highest association with lower QoL (Table 2). Nutritional care needs and receiving nutritional care were also associated with lower QoL. Age, sex, and treatment adjusted multivariable linear regression analysis showed that having clinically important gastrointestinal problems ($\beta = -12.9$ (95% CI $(-15.5$ to $-10.3)$)), receiving nutritional care ($\beta = -5.1$ (95% CI $(-8.5$ to $-1.7)$)), and

Fig. 1 Flow diagram of study inclusion

having nutritional care needs ($\beta = -8.7$ (95% CI (-11.9 to -5.5))) were independently associated with a lower QoL. This also holds for non-clinically important gastrointestinal problems, although the association was less strong (Table 2). No collinearity was present in the model (VIF for all variables was <10).

Discussion

This study showed that almost 50% of patients with advanced cancer had clinically important gastrointestinal problems, while only 14% received nutritional care. Having clinically important or non-clinically important gastrointestinal problems, nutritional care needs, and received nutritional care were independently associated with a lower QoL. This

might be explained by reverse causality, as patients with more and more severe gastrointestinal symptoms (and associated lower QoL) are more often referred to a dietitian. This reverse causation is also present with the other healthcare professionals, in other words patients receiving care of other healthcare professionals have a lower QoL than patients who did not receive care.

To the best of our knowledge, there are no studies investigating the combined associations of gastrointestinal problems, received nutritional care, and nutritional care needs with QoL in patients with advanced cancer. Only studies investigating the univariable association between gastrointestinal problems or nutritional care needs and QoL were found [7, 8, 19]. Studies investigating the association between gastrointestinal problems and QoL in advanced cancer showed that appetite loss, nausea, vomiting, and

Table 1 Socio-demographic and clinical characteristics of patients with advanced cancer, by having gastrointestinal problems ($n = 1080$)

	Total study population $N = 1080$	Clinically important gastro- intestinal problems $N = 536$	Non-clinically important gastrointestinal problems $N = 167$	No gastrointestinal problems $N = 366$
	Mean \pm SD or number (%)	Mean \pm SD or number (%)	Mean \pm SD or number (%)	Mean \pm SD or number (%)
Age ^a , (years)	65.2 \pm 9.8	65.0 \pm 9.7	64.5 \pm 10.3	65.6 \pm 9.8
Sex				
Male	552 (51%)	272 (51%)	78 (47%)	194 (53%)
Relationship status ^b				
Having a partner	895 (83%)	436 (81%)	134 (81%)	315 (86%)
Single	184 (17%)	100 (19%)	32 (19%)	51 (14%)
Education level ^c				
Low	320 (30%)	184 (35%)	48 (29%)	84 (23%)
Medium	441 (41%)	209 (40%)	63 (38%)	164 (45%)
High	309 (29%)	136 (26%)	55 (33%)	116 (32%)
Tumor type ^d				
Lung	314 (29%)	150 (28%)	47 (29%)	114 (32%)
Breast	150 (14%)	72 (14%)	35 (21%)	57 (16%)
Colorectal	197 (18%)	108 (20%)	35 (21%)	50 (14%)
Prostate	127 (12%)	54 (10%)	18 (11%)	52 (14%)
Other	278 (26%)	149 (28%)	28 (18%)	86 (24%)
Treatment in the last month ^e				
No	60 (6%)	25 (7%)	10 (6%)	23 (4%)
Yes	1016 (94%)	339 (93%)	157 (94%)	511 (96%)
Radiotherapy	141 (13%)	72 (13%)	25 (15%)	44 (12%)
Chemotherapy	650 (61%)	173 (47%)	107 (64%)	370 (69%)
Surgery	36 (3%)	26 (5%)	2 (1%)	8 (2%)
Immunotherapy	297 (26%)	137 (10%)	47 (28%)	113 (31%)
Other	205 (19%)	92 (17%)	28 (17%)	85 (23%)
Gastrointestinal symptoms and quality of life				
Nausea/vomiting	9.4 \pm 18	19 \pm 21	0	0
Appetite loss	19 \pm 27	32 \pm 31	17 \pm 17	0
Constipation	13 \pm 23	20 \pm 28	21 \pm 16	0
Diarrhea	12 \pm 23	25 \pm 28	0	0
Global QoL	68 \pm 20	62 \pm 20	69 \pm 19	76 \pm 17
Received nutritional care ^{f*}				
Yes	142 (14%)	92 (19%)	21 (14%)	25 (8%)
Nutritional care needs ^{g*}				
Yes	67 (6%)	48 (9%)	10 (6%)	8 (2%)
A little bit	109 (10%)	60 (12%)	15 (9%)	32 (10%)
No	869 (83%)	413 (79%)	137 (85%)	314 (89%)

Missing values: a: 3, b: 1, c: 10, d: 14, e: 4, f: 79, g: 35. Variables may deviate from 100% due to rounding off. Received nutritional care and nutritional care needs were tested using χ^2

SD standard deviation

* $p < 0.05$

constipation were significantly associated with a lower QoL [7, 8, 19]. Compared to our results, the severity of these gastrointestinal problems (mean scores ranging from 7 to 14 for nausea and vomiting, 23–43 for appetite loss, 13–32 for constipation, and 6–19 for diarrhea) was in line

for nausea/vomiting and diarrhea but higher for appetite loss and constipation than in our study [20–23]. Moreover, QoL was also lower when appetite loss and nausea/vomiting occurred concurrently, compared to patients unaffected by these symptoms [24, 25]. Moreover, the difference in

Table 2 Associations of gastrointestinal problems, nutritional care, and nutritional care needs with quality of life

Global QoL	Univariable model			Unadjusted multivariable model ^b			Adjusted multivariable model ^c		
	β	Lower bound 95% CI	Upper bound 95% CI	β	Lower bound 95% CI	Upper bound 95% CI	β	Lower bound 95% CI	Upper bound 95% CI
Nausea/vomiting									
Clinically important	12.1	-14.6	-9.7						
Non-clinically important	-	-	-						
Appetite loss									
Clinically important	-22.8	-26.1	-19.6						
Non-clinically important	-10.9	-13.5	-8.3						
Constipation									
Clinically important	-10.2	-14.8	-5.6						
Non-clinically important	-5.9	-8.7	-3.04						
Diarrhea									
Clinically important	-8.6	-11.2	-5.9						
Non-clinically important	-	-	-						
Gastrointestinal problems ^a									
Clinically important	-14.1	-16.6	-11.5	-12.9	-15.5	-10.3	-12.9	-15.5	-10.3
Non-clinically important	-6.6	-10.1	-3.1	-6.4	-10.0	-2.8	-6.5	-10.1	-2.9
Received nutritional care									
Nutritional care needs	-7.3	-10.9	-3.8	-5.1	-8.5	-1.7	-5.1	-8.5	-1.7
	-10.1	-13.3	-6.9	-8.6	-11.7	-5.4	-8.7	-11.9	-5.5

CI confidence interval

^aNo gastrointestinal problems was set as the reference category

^bMultivariable regression model including gastrointestinal problems, received nutritional care, and nutritional care needs (no collinearity was present)

^cMultivariable regression model including gastrointestinal problems, received nutritional care, and nutritional care needs, adjusted for age, sex, and treatment yes/no (no collinearity was present)

global QoL between patients with clinically relevant nutritional problems and no nutritional problems is considered medium, while the difference between clinically and not clinically relevant nutritional problems is small, according to Cocks et al. [26].

In our study, nutritional care needs were also associated with lower QoL which is in line with the results of 18 qualitative studies described in the review of Wheelwright et al. [27]. A study in patients with advanced cancer showed that these patients often seek information regarding nutrition hoping to restore their QoL [28]. Moreover, a study performed in cancer patients undergoing chemotherapy further affirms our findings [29] showing a lower QoL in patients needing nutritional counseling compared to patients who did not need it.

Only preliminary studies have shown that nutritional support may be associated with beneficial effects, i.e., prevented bedsores [12], improved performance status [13] in the very advanced cancer patients but these studies have not specifically looked at QoL. The intervention consisted of providing individualized and tailored nutritional support to meet or exceed the energy and protein requirements. Besides

nutritional advice to improve nutritional intake, dietitians may also play an important role in supporting psychosocial consequences of nutritional problems of patients and their informal caregivers especially when emotions lead to conflicts in the patient-informal caregiver relationship. In a pilot randomized controlled trial [30], advanced cancer patients and family caregivers were randomized either to receive 2–3 h of direct dietitian contact time over a 4–6-week period, or to the control group receiving only usual care. During the intervention, issues with nutrition impact symptoms and food or eating-related psychosocial concerns were addressed through nutrition counseling, with a focus on improving nutrition-related communication between the dyads. Results showed improvement in quality of life, eating-related distress, and eating-related enjoyment in a subgroup of patients. However, these preliminary results should be interpreted with caution because compliance in this pilot study was poor; of the 89 eligible patients, 42 were randomized and only 20 finished the 5-week assessment.

The present work covers a novel topic of research showing that gastrointestinal problems (both severe and less severe) and nutritional care needs are independently associated

with lower QoL. These findings highlight the importance of addressing gastrointestinal problems as a standard part of daily care for advanced cancer patients in order to optimize symptom management probably by a combination of nutritional care, pharmacological and psychosocial interventions.

Some limitations of this study need to be addressed. First, although the response rate was high (65%), generalizability of our results may be limited because compared to all patients who died of cancer in the Netherlands, patients in our study were more often male, younger, and more likely to have been diagnosed with prostate or breast cancer. Also, patients with worse health status might be less often included in our study (selection bias), leading to a potential overestimation of QoL and underestimation of symptoms [31]. Second, due to the cross-sectional character of the study, this study cannot investigate causality. It is possible that the observed associations of gastrointestinal problems, lack of nutritional care, and nutritional care needs with QoL might be bidirectional. Third, some residual confounding is to be expected. Studies show that weight loss, physical function, physical activity, and systemic inflammatory response in patients with advanced cancer may have an effect on QoL and be associated with gastrointestinal problems [32, 33]. Unfortunately, no information about these factors was available.

Future research should further investigate the relationship between gastrointestinal problems, nutritional care, and nutritional care needs with QoL in a longitudinal setting, including all relevant information. Next, specifically the effect of symptom management strategies for gastrointestinal problems such as nutritional care (e.g., diet modifications), but also pharmacological and psychosocial interventions for nutritional issues, should be investigated in prospective randomized trials, as these problems are of paramount importance for the QoL of patients with advanced cancer.

Conclusion

More than half of all patients with advanced cancer experience gastrointestinal problems, while only few patients receive nutritional care. These gastrointestinal problems, nutritional care needs, and received nutritional care are associated with lower quality of life. More prospective cohort studies and randomized studies are needed to clarify the role of nutritional counseling on gastrointestinal problems, psychosocial well-being, and QoL in patients with incurable cancer.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s00520-023-07646-1>.

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Data availability Since 2011, PROFILES registry data is freely available according to the FAIR (Findable, Accessible, Interoperable, Reusable) data principles for non-commercial (international) scientific research, subject only to privacy and confidentiality restrictions. The datasets analyzed during the current study are available through Questacy (DDI 3.x XML) and can be accessed by our website (www.profilesregistry.nl). In order to arrange optimal long-term data warehousing and dissemination, we follow the quality guidelines that are formulated in the “Data Seal of Approval” (www.datasealofapproval.org) document, developed by Data Archiving and Networked Services (DANS). The data reported in this manuscript will be made available when the eQuiPe study is completed.

Author contribution SP, NL, SE, SB, LP, and NR were involved in the study design. SP drafted the manuscript and performed the statistical analysis. All authors reviewed the manuscript and gave final approval of the manuscript.

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Declarations

Ethical approval This study was performed in line with the principles of the Declaration of Helsinki. The study was reviewed by the Medical Research Ethics Committee of the Antoni van Leeuwenhoek hospital in the Netherlands (METC17.1491).

Consent to participate Written informed consent was obtained from all individual participants included in the study.

Consent for publication Written informed consent was obtained from all individual participants included in the study.

Conflict of interest The authors declare no competing interests.

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